

# Epitomes

## Important Advances in Clinical Medicine

### Occupational Medicine

*The Scientific Board of the California Medical Association presents the following inventory of items of progress in occupational medicine. Each item, in the judgment of a panel of knowledgeable physicians, has recently become reasonably firmly established, both as to scientific fact and important clinical significance. The items are presented in simple epitome and an authoritative reference, both to the item itself and to the subject as a whole, is generally given for those who may be unfamiliar with a particular item. The purpose is to assist busy practitioners, students, research workers or scholars to stay abreast of these items of progress in occupational medicine that have recently achieved a substantial degree of authoritative acceptance, whether in their own field of special interest or another.*

*The items of progress listed below were selected by the Advisory Panel to the Section on Occupational Medicine of the California Medical Association and the summaries were prepared under its direction.*

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#### Irritant and Sensitization Effects of Formaldehyde

CLINICIANS NOT UNCOMMONLY ENCOUNTER patients with concerns about the relationship of a variety of subjective symptoms and formaldehyde exposure and sensitivity at home or in the workplace.

In October 1983 the Consensus Workshop on Formaldehyde brought together scientists from academia, government and industry to address the toxicology of formaldehyde. The workshop's panel on Immunology, Sensitization and Irritation reaffirmed that irritation of the eye and upper respiratory tract occurs but that a population threshold for this effect does not exist. Some sensitive persons may have sensory irritation at formaldehyde concentrations as low as 0.03 ppm, though most do not until levels are greater than 0.1 ppm. The ability of formaldehyde to produce skin irritation and allergic contact dermatitis was affirmed. Formaldehyde-induced contact urticaria has been documented on both an immune (type I allergy) and nonimmune basis. The workshop did not feel that sufficiently well-controlled scientific studies were available to establish that respiratory tract sensitization to formaldehyde occurs.

Pulmonary sensitization to formaldehyde may occur but is probably rare. In 1984 Reed and co-workers published a report of 13 patients with symptoms suggestive of asthma who had been exposed at home or work to formaldehyde ranging from 0.1 to 1.2 ppm. On bronchial challenge with 0.1, 1 and 3 ppm of formaldehyde for 20 minutes, no patient showed a significant (20% or greater) decline in forced expiratory volume in one second over 24 hours. Similar findings have been noted in persons with asthma, suggesting that even in preexisting asthmatic conditions formaldehyde at these concentrations fails to induce bronchial hyperactivity on an irritant basis. These reports contrast with that of Nordman and colleagues in 1985. A total of 230 patients occupationally

exposed to formaldehyde was referred to the Institute of Occupational Health from all over Finland. Detailed medical and occupational histories were taken, spontaneous diurnal variations of peak expiratory flow were recorded and spirometry with bronchodilator, histamine provocation tests and bronchial challenges with 1 to 2 ppm formaldehyde and placebo were done. Of the 230 patients, 12 were considered to have bronchial asthma specifically caused by formaldehyde.

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#### REFERENCES

- Frigas E, Filley WV, Reed CE: Bronchial challenge with formaldehyde gas: Lack of bronchoconstriction in 13 patients suspected of having formaldehyde-induced asthma. *Mayo Clin Proc* 1984 May; 59:295-299
- Nordman H, Keskinen H, Tuppurainen M: Formaldehyde asthma—Rare or overlooked? *J Allergy Clin Immunol* 1985 Jan; 75:91-99
- Report of the Consensus Workshop on Formaldehyde. *Environ Health Perspect* 1984 Dec; 58:323-381

#### Evaluating Infertility—Occupational Dangers to the Male Reproductive System

IN AN EARLIER ISSUE of the journal, Becker described male reproductive hazards, and this topic was later extended to workplace exposure. I will discuss two generally accepted approaches to evaluating gonadotoxic effects of occupational agents: assessing sperm quality and monitoring worker reproductive history by a brief questionnaire.

Full clinical assessment of sperm quality involves consideration of many complex factors. Examination of one of these factors, sperm count, has been the major sperm-related method for evaluating the workplace for gonadotoxic agents. As described by Whorton and co-workers, however, the method is psychologically invasive because one or more sperm specimens are required for analysis. Other important limitations and methodologic problems are discussed by Milby and Whorton. The method's principal advantage is that combining sperm count data with environmental exposure

measurements often shows recent contact with gonadotoxic agents.

Worker reproductive history is monitored by a questionnaire. This method involves retrospectively computing a standardized fertility ratio (SFR) derived from data on national birth probabilities. The SFR describes fertility before, during and after gonadotoxic exposure and differences are identified between exposed and nonexposed groups. A major advantage is its essentially noninvasive nature: questionnaire responses are limited to psychologically benign factors such as marital status, date of marriage and number, age and sex of children. Levine and colleagues have validated this method among workers exposed to dibromochloropropane and concluded that the questionnaire technique would have identified damage to the male reproductive system a number of years earlier than did the sperm count method.

Both methods generate valuable screening and evaluation data. The major difference is that the sperm count method is more useful for identifying recent gonadotoxic exposures, whereas the questionnaire approach provides a retrospective picture of male reproductive system damage. Both methods, however, provide useful tools for assessing the gonadotoxic potential of a workplace.

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#### REFERENCES

- Becker CE: Male reproductive hazards (Epitomes of Progress). *West J Med* 1983 Aug; 139:212
- Levine RJ, Blunden PB, DalCorso RD, et al: Superiority of reproductive histories to sperm counts in detecting infertility at a dibromochloropropane manufacturing plant. *J Occup Med* 1983 Aug; 25:591-597
- Levine RJ, Symons MJ, Balogh SA, et al: A method for monitoring the fertility of workers—2. Validation of the method among workers exposed to dibromochloropropane. *J Occup Med* 1981 Mar; 23:183-188
- Milby TH, Whorton D: Epidemiological assessment of occupationally related, chemically induced sperm count suppression. *J Occup Med* 1980 Feb; 22:77-82
- Whorton D, Milby TH, Krauss RM, et al: Testicular function in DBCP exposed pesticide workers. *J Occup Med* 1979 Mar; 21:161-166

## Silicosis and Cancer Risk

ALTHOUGH THE ASSOCIATION between asbestos exposure and lung cancer has been well documented, silica exposure has not generally prompted concern about the excess risk of lung cancer. Recent evidence from both epidemiologic investigations and studies using animals has stimulated renewed interest in this association.

The findings of several studies of miners and foundry workers suggest that they have an excess risk of lung cancer. Those with relatively heavy exposure, such as furnace bricklayers and fettlers, appear to have the highest risk of excess lung cancer deaths. The specific role of silica is difficult to interpret, however, in that foundry workers are exposed to several potentially carcinogenic agents, such as polycyclic aromatic hydrocarbons (PAH), other organic compounds and metals such as lead, chromium and nickel. Some recent data suggest that there may be a synergistic interaction between silica and PAH in increasing the risk of lung and urogenital cancer. There is one group of workers, Vermont granite workers, who have a relatively isolated exposure to silica dust. Data from a 30-year cohort study of mortality in these workers suggest a slight but not significant increase in the incidence of cancer of the respiratory and gastrointestinal tracts and prostate and no relationship between amount of silica exposure and cancer risk.

Recent studies in animals suggest that silica alone may be a carcinogen. It appears that lifetime studies may be necessary to show tumorigenesis; perhaps this is why the association between silica and cancer has not been appreciated in earlier studies of experimental silicosis. Adenocarcinomas and squamous cell carcinomas have been induced in rats after either inhalational exposures or intratracheal instillations. Histiocytic tumors have been induced in rats by intrapleural inoculation of silica, which has also been found to act as a cocarcinogen with benzpyrene.

In summary, then, if there is an increased risk of lung cancer from silica, the risk is probably small and will be very difficult to prove conclusively. Important confounding variables in epidemiologic studies include smoking history, the concomitant presence of nonmalignant respiratory tract disease and occupational exposure to other dusts and carcinogens. Though studies in animals suggest that silica may be a carcinogen, there is a long latency, relatively heavy exposure may be necessary to elicit tumorigenesis and species specificity may be significant. Whether silica acts as a carcinogen alone, as a cocarcinogen or in some other capacity to enhance the risk of lung cancer remains to be determined. As new data emerge, evaluation of silica exposure standards may need to take into account the role of silica exposure in lung cancer risk.

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#### REFERENCES

- Davis LK, Wegman DH, Monson RR, et al: Mortality experience of Vermont granite workers. *Am J Ind Med* 1983; 4:705-723
- Goldsmith DF, Guidotti TL, Johnston DR: Does occupational exposure to silica cause lung cancer? *Am J Ind Med* 1982; 3:423-440
- Goldsmith DF, Winn DM, Shy CM (Eds): *Silica, Silicosis and Cancer: Controversy in Occupational Medicine*. Philadelphia, Praeger, 1985
- Palmer WG, Scott WD: Lung cancer in ferrous foundry workers: A review. *Am Ind Hyg Assoc J* 1981 May; 42:329-340

## Surveillance of Hospital Personnel Exposed to Cytotoxic Drugs

MANY CYTOTOXIC DRUGS have been shown to be carcinogens or mutagens. In recent years, there has been a pronounced increase in the use of cytotoxic agents in treating cancer patients and, infrequently, patients with collagen diseases and psoriasis. In some patients who have had cytotoxic therapy, new malignant tumors have developed. Exposure to these drugs may prove to be occupationally health-hazardous in the case of certain hospital workers. Hospital pharmacists are involved in handling and preparing cytotoxic drugs, nurses and physicians in their administration and housekeeping staff in disposing of drug residues and products.

A few studies have been conducted relating chronic daily exposure to small amounts of these drugs to possible mutagenic or carcinogenic effects in the population at risk. Two methods have been used in assessing exposure to the cytotoxic drugs. First, the measurement of mutagenic activity in urine and, second, chromosome analysis for sister chromatid exchange and other chromosome aberrations of peripheral lymphocytes. Most studies indicate that personnel who were exposed to cytotoxic drugs had a greater number of chromosome abnormalities and increased sister chromatid exchanges or an increase in urine mutagenic activity.

Although these methods of assessing exposure to cytotoxic drugs have their limitations, and while better surveillance